REMARKS

In the Office Action of March 21, 2003, Claims 6 - 17 were rejected. In response, Claims 7 - 9, 11 - 13 and 15 - 17 are canceled without prejudice or disclaimer, Claims 6, 10 and 14 are amended and new Claims 18 and 19 are added to the application. Reexamination and reconsideration are respectfully requested in view of the following remarks.

Amendment to the Specification and Claims

The specification is amended to provide a replacement for Table 1 on page 7. In particular, the new table eliminates the erroneous double bonds from the xanthine core of the compounds. It is respectfully submitted that persons skilled in the art would immediately recognize that the original table contain the errors, and the corrected as submitted herewith would be immediately apparent. Accordingly, it is respectfully submitted that this amendment does not introduce new matter into the specification.

Claims 6, 10 and 17 are amended to be directed to Compound 1 as shown in Table 1 on page 7 of the specification.

New Claim 18 is directed to a method of treating brain ischemia and is supported on page 13, line 5 of the specification. New Claim 19 is directed to a method of inhibiting dopaminergic neurodegeneration and is supported by Test Example 1, beginning on page 9 of the specification.

Objection to Claim 8

Claim 8 was objected to. This objection is moot, since Claim 8 is canceled.

Rejection of Claims 6 - 17 under 35 U.S.C. §112, first paragraph

Claims 6 - 17 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that is not described in the specification so as to enable one skilled in the art to practice the invention. The Examiner acknowledges that support is provided for the inhibitory activity on degeneration of dopamine neurons following administration of Compounds 1, 2, 3 and 4, but alleges that undue experimentation would be required to practice the claimed method.

In response, Claims 6, 10 and 14 are amended to be limited to Compound 1 of Table 1 on page 7 of the specification. Applicants respectfully submit that a person skilled in the art could practice the methods of the claimed invention with Compound 1 without undue experimentation. In support thereof, applicants submit data showing the protective activity of Compound 1 against cerebral ischemia and present journal articles showing the relation between an inhibitory action on degeneration of dopaminergic neurons and the possibilities of treating diseases encompassed by the term "neurodegeneration". A Form PTO-1449 is provided to list the references submitted herewith.

These references show that compounds having inhibitory action on degeneration of dopaminergic neurons are useful for treatment of diseases encompassed by the term "neurodegeneration". In particular, Saporito, Glicksman, Olson and Vajda show a relation between an inhibitory action on degeneration of dopaminergic neurons and treatment of Alzheimer's disease, amyotrophic lateral sclerosis and/or multi-system atrophy. Kim, Jenner, and Emerich show a relation between an inhibitory action on degeneration of dopaminergic neurons and treatment of progressive supranuclear palsy, multi-system atrophy and/or

Huntington's chorea. Gray and Shor-Psner show a relation between an inhibitory action on degeneration of dopaminergic neurons and treatment of AIDS brain fever.

Accordingly, persons skilled in the art would be enabled to practice the invention as defined in the present claims. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, with respect to amended Claims 6, 10 and 14 and new Claims 18 and 19 is therefore respectfully requested.

Rejection of Claims 6 - 17 under 35 U.S.C. §103(a) over Baraldi

Claims 6 - 17 were rejected under 35 U.S.C. §103(a) as obvious over Baraldi et al, Current Medicinal Chemistry, 2/3 (707-722) 1995 (abstract). The Examiner alleges that Baraldi teaches compounds of instant formula I for use in the treatment of cerebral ischemia or neurodegenerative disorders and to improve learning and enhance cognition. Although the Examiner acknowledges that Baraldi lists only Parkinson's disease as a neurodegenerative disorder, the Examiner takes the position that it would be obvious to use the 8-styrylxanthines of Baraldi to treat other neurodegenerative disorders.

In response, Claims 6, 10 and 14 are amended to be directed to Compound 1 of Table 1 of the application. This compound is not disclosed in Baraldi, which does not teach or suggest any xanthine derivatives having ethyl groups in the 1- and 3-positions. The closest compound to compound 1 of the present application that is disclosed in Baraldi is a compound referred to as Compound 10, disclosed in Table 3 of Baraldi. Applicants provide a Declaration of Shunji Ichikawa under 37 CFR 1.132 presenting data showing that the protective activity against cerebral ischemia of Compound 1 of the present application is markedly superior to that of Compound

10 disclosed in Table 3 of Baraldi.

Accordingly, it is respectfully submitted that Claims 6, 10 and 14 as amended herein, and new Claims 18 and 19 would not have been obvious over Baraldi.

Rejection of Claims 6 - 17 under 35 U.S.C. §103(a) over Suzuki

Claims 6 - 9 were rejected under 35 U.S.C. §102(b) as anticipated by Suzuki, U.S. Patent No. 5,484,940. The Examiner alleges that Suzuki teaches compounds of instant formula I for use in the treatment of senile dementia.

In response, Claims 6, 10 and 14 are amended to be directed to Compound 1 of Table 1 of the application. This compound is not disclosed in Suzuki, which does not teach or suggest any xanthine derivatives having only methoxy as substituents on the styryl moiety. The closest compound to compound 1 of the present application that is disclosed in Suzuki is a compound referred to as Compound 5, disclosed in the Table on page 6 of Suzuki. Applicants provide a Declaration of Masako Kurokawa under 37 CFR 1.132 presenting data showing that the inhibitory action against cerebral ischemia of Compound 1 of the present application is markedly superior to that of Compound 5 disclosed on page 6 of Suzuki.

Accordingly, it is respectfully submitted that Claims 6, 10 and 14 as amended herein, and new Claims 18 and 19 would not have been obvious over Suzuki.

Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 6, 10 and 14, and new Claims 18 and 19 are in condition for allowance. Favorable reconsideration is respectfully requested.

Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 01-2135. (File No. 506.38266CX1).

Respectfully submitted,

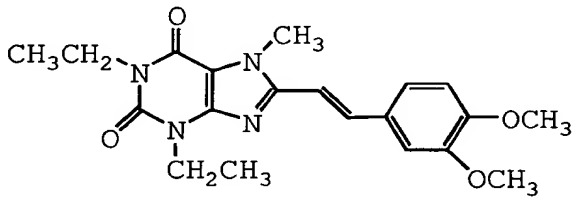
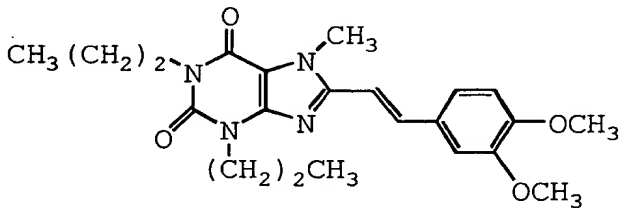
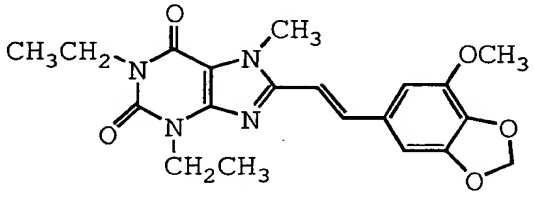
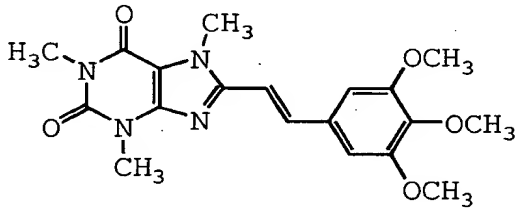
ANTONELLI, TERRY, STOUT & KRAUS, LLP

Ralph T. Webb
Registration No. 33,047

RTW/RTW
Tel.: 703-312-6600
Fax.: 703-312-6666
Attachments:
Amended Table 1
Original Table 1 showing changes made
Form-1449 with attached documents
Declaration of Shunji Ichikawa
Declaration of Masako Kurokawa

1. Please replace Table 1 on page 7 with the following table.

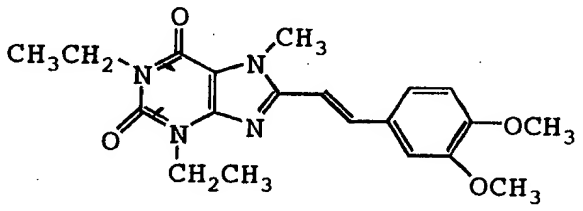
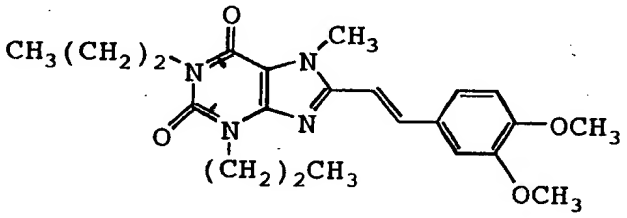
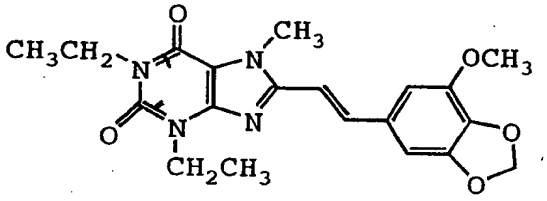
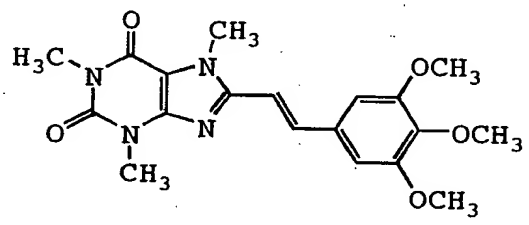
Table 1

Compound No.	
1	
2	
3	
4	

Marked-up copy to show changes made

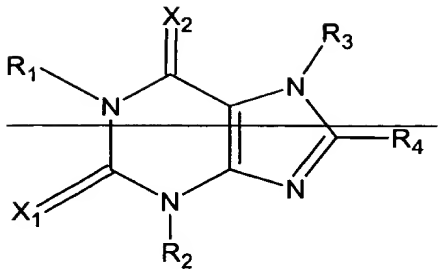
IN THE SPECIFICATION

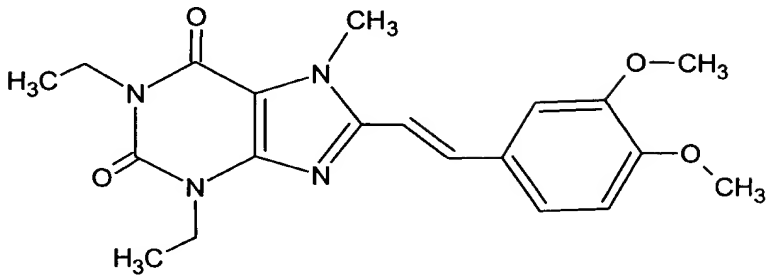
Table 1

Compound No.	
1	
2	
3	
4	

IN THE CLAIMS

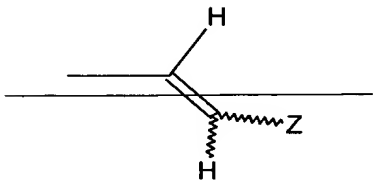
6. (three times amended) A method of inhibiting neurodegeneration except Parkinson's disease, which comprises administering an effective dose of a xanthine derivative represented by formula (I):



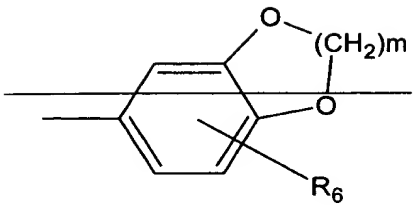


(I)

~~wherein X_1 and X_2 independently represent O or S, R_1, R_2 and R_3 independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl; R_4 represents the following group:~~

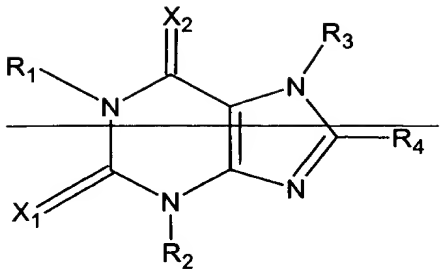


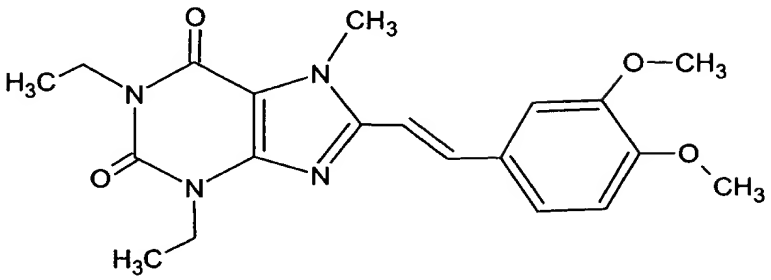
~~wherein Y_1 and Y_2 independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:~~



~~wherein m is an integer of 1 to 3 and R_6 represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, trifluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl;~~ or a pharmaceutically acceptable salt thereof~~, as an active ingredient~~.

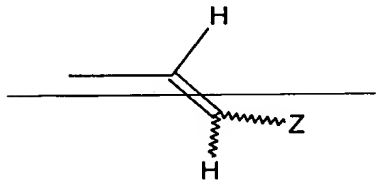
10. (twice amended) A method of treating neurodegenerative disorders except for Parkinson's disease ~~and attention deficit hyperactivity disorder~~, which ~~method~~ comprises administering an effective dose of a xanthine derivative represented by formula (I):



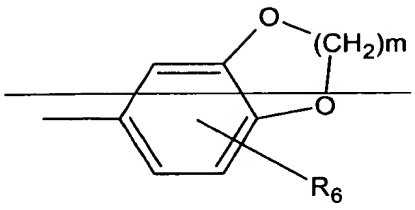


(I)

~~wherein X_1 and X_2 independently represent O or S, R_1, R_2 and R_3 independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl; R_4 represents the following group:~~

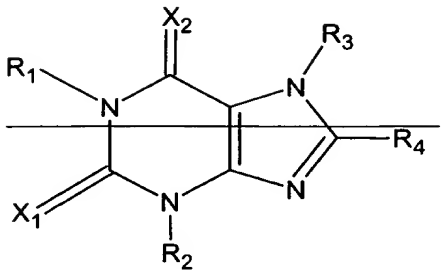


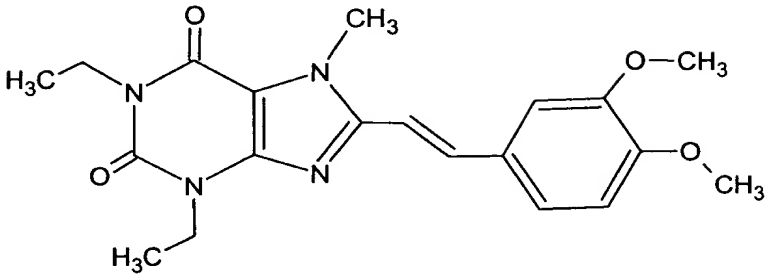
~~wherein Y_1 and Y_2 independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:~~



~~wherein m is an integer of 1 to 3 and R_6 represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, trifluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl;~~ or a pharmaceutically acceptable salt thereof~~, as an active ingredient~~.

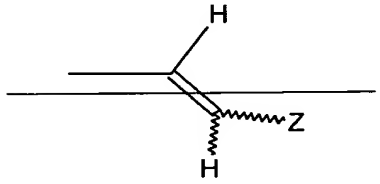
14. (twice amended) A method of treating Alzheimer's disease, which comprises administering an effective dose of the xanthine derivative represented by formula (I):



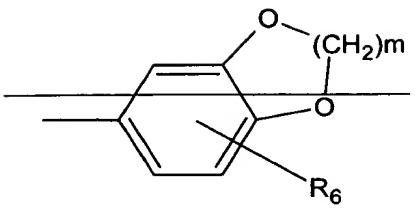


(I)

~~wherein X_1 and X_2 independently represent O or S, R_1, R_2 and R_3 independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl; R_4 represents the following group:~~



~~wherein Y_1 and Y_2 independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:~~



~~wherein m is an integer of 1 to 3 and R_6 represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, trifluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl;~~ or a pharmaceutically acceptable salt thereof~~, as an active ingredient~~.